PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 18 June 2001 (18.06.01)	
International application No. PCT/EP00/09455	**Applicant's or agent's file reference** 4-31158A
International filing date (day/month/year) 27 September 2000 (27.09.00)	**Priority date** (day/month/year) 29 September 1999 (29.09.99)
Applicant SHAH, Rajen et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

26 March 2001 (26.03.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Olivia TEFY
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

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From the INTERNATIONAL BUREAU

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NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

BECKER, Konrad
Novartis AG
Corporate Intellectual Property
Patent & Trademark Dept.
CH-4002 Basel
SUISSE

Date of mailing (day/month/year)
18 September 2001 (18.09.01)

Applicant's or agent's file reference
4-31158A

IMPORTANT NOTIFICATION

International application No.
PCT/EP00/09455

International filing date (day/month/year)
27 September 2000 (27.09.00)

1. The following indications appeared on record concerning:

[X] the applicant [ ] the inventor [ ] the agent [ ] the common representative

Name and Address
NOVARTIS AG
Schwarzwaldallee 215
CH-4058 Basel
Switzerland

State of Nationality: CH
State of Residence: CH
Telephone No.:
Facsimile No.:
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

Name and Address
NOVARTIS AG
Lichtstrasse 35
CH-4056 Basel
Switzerland

State of Nationality: CH
State of Residence: CH
Telephone No.:
Facsimile No.:
Teleprinter No.:

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[X] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
Dominique DELMAS

Telephone No.: (41-22) 338.83.38

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(74) Agent: **BECKER, Konrad**; Novartis AG, Corporate Intellectual Property, Patent & Trademark Dept., CH-4002 Basel (CH).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

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Published:
— *with international search report*

(48) Date of publication of this corrected version:
26 July 2001

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see PCT Gazette No. 30/2001 of 26 July 2001, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/22944 A1

(54) Title: ORAL CONTROLLED RELEASE FORMULATIONS

(57) Abstract: Pharmaceutical composition capable of releasing a therapeutically effective dose of active agent, e.g., rivastigmine, in a time-controlled manner. The pharmaceutical composition comprises a core containing a pharmacologically active agent, and a coating wherein the coating comprises an outer film and an inner film, the inner being in the form of a membrane which is semi-permeable to water or body fluids.

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
4-31158A		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP00/09455	27/09/2000	29/09/1999
International Patent Classification (IPC) or national classification and IPC A61K9/22		
Applicant NOVARTIS AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
26/03/2001	09.01.2002
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Epskamp, S Telephone No. +31 70 340 2857

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/09455

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-39 as originally filed

Claims, No.:

1-7 with telefax of 31/10/2001

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-7
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-7
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-7
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:

D1: EP-A-0 621 032
D2: WO-A-99/01121
D3: EP-A-0 612 520
D4: DE-A-38 05 744

The documents D4 was not cited in the international search report. A copy of the document is appended hereto.

Document D4 can be regarded as the closest state of the art, as it discloses (page 3, lines 10-41; example 1; claims 1-9) (S)-N-ethyl-3-[(dimethylamino)ethyl]-N-methyl phenyl carbamate (rivastigmine) and medical uses thereof. Although it is disclosed that the compound is orally active (page 5, lines 57-58), no suggestions are made for a specific pharmaceutical form.
Generally, forms as claimed in claim 1 are known from e.g. D1-D3. However, no suggestion is made in these documents to use these forms for the administration of rivastigmine.
Therefore it was not obvious for the person skilled in the art to formulate rivastigmine in a composition according to present claim 1, to solve the problem of providing a controlled release oral composition of rivastigmine.
Thus present claims 1-7 are regarded as novel and inventive with respect to D1-D4.

Re Item VI

Certain documents cited

WO-A-00/19985 was cited in the search report as an intermediate document. However it appears that this document has no valid priority for the subject-matter relating to the subject-matter of present claims, except for the subject-matter of example 2 disclosed therein.

Claims

1. Pharmaceutical composition comprising
a core containing Rivastigmine as a pharmaceutically active agent, and
a coating
wherein the coating comprises an inner film and an outer film.

2. Pharmaceutical composition according to claim 1 wherein the inner film is in the form of a membrane which is semi-permeable to water or body fluids.

3. Pharmaceutical composition according to claim 1 or 2 wherein the outer film is permeable to water or body fluids.

4. Pharmaceutical composition according to any one of claims 1 to 3 wherein the coating has a thickness of 50 to 800 micrometers.

5. A pharmaceutical composition according to any one of claims 1 to 4 wherein said core releases an effective dose of the active agent 6 to 12 hours after ingestion.

6. A two pulse release pharmaceutical composition comprising a composition according to any one of claims 1 to 5.

7. Use of Rivastigmine and excipients as defined in any one of claims 1 to 6 in the manufacture of a medicament for the treatment of patients with mild to moderately severe Dementia of the Alzheimer's type by oral administration.